

PATENT

Our Docket: P-LA 1245

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of  
Border and Ruoslahti

Serial No.: 08/349,479

Filed: December 2, 1994

For: INHIBITING TRANSFORMING  
GROWTH FACTOR- $\beta$  TO  
PREVENT ACCUMULATION OF  
EXTRACELLULAR MATRIX

)  
)  
) Examiner: P. Gambel

)  
) Group Art Unit: 1644

) I hereby certify that this correspondence is being deposited with  
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Washington, D.C. 20231

October 22, 2001

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**EXHIBIT 1**

**DECLARATION PURSUANT TO 37 C.F.R § 1.132**

**EXECUTED 10/13/01,**

**WITH ATTACHED EXHIBITS A, B AND C**



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DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Sir:

I, Wayne Border, M.D., declare as follows:

1. I am a co-inventor of the subject matter which is described and claimed in the above-identified patent application.

2. I have previously executed Declarations pursuant to 37 C.F.R. § 1.131 on October 1, 1996, and on August 25, 1999, in connection with the above-identified application. Copies of the Rule 131 Declarations of October 1, 1996, and August 25, 1999, are attached hereto as Exhibits A and B, respectively.

3. The Rule 131 Declarations of October 1, 1996, and August 25, 1999, contain as Exhibit D and B1, respectively, a copy of the August 8, 1988, laboratory notebook entry from the laboratory notebook I kept from February 1988 until October 1988.

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The Rule 131 Declarations of October 1, 1996 and August 25, 1999, accurately describe the experimental data depicted in Exhibit D and B1, respectively, and further accurately indicate that the corresponding experiments were performed prior to April 1, 1989 and December 22, 1988 respectively. However, as explained below, not all of the handwritten notations present on Exhibit D and B1 to the aforementioned Declarations originated prior to December 22, 1988.

4. Attached as Exhibit C to this Declaration is a copy of the original laboratory notebook entry of August 8, 1988, as it appears in the laboratory notebook I kept from February 1988 until October 1988. The upper right hand legend present on Exhibit D and B1, respectively to the aforementioned Declarations, is not present in the original notebook entry. The discrepancy between the original laboratory notebook entry and the copy that was submitted as Exhibit D and B1, respectively, to the aforementioned Rule 131 Declarations arose when I added the legend found in the upper right hand margin for the purpose of explaining the abbreviations and shorthand notations present in the original. Specifically, during prosecution of the above-identified application, I was asked by a representative of the Assignee for documentary evidence showing the conception of the use of anti-TGF $\beta$  to inhibit extracellular matrix accumulation. Prior to faxing the laboratory notebook page that became Exhibit D and B1 to the attached Rule 131 Declarations, I added the upper right hand legend to more easily explain the depicted experimental data to a person unfamiliar with the shorthand notations and abbreviations used in my laboratory notebook. At

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the time I added the upper right hand legend to the copy of my laboratory notebook entry of August 8, 1988, I did not appreciate that the copy containing the added notation would become an actual Exhibit.


5. The upper right hand legend present in Exhibit D and B1, respectively, to the attached Rule 131 Declarations provides an accurate description of the data depicted in my original August 8, 1988, notebook entry provided as Exhibit C. The relevant panel with regard to the experiments aimed at characterizing the role of anti-TGF- $\beta$  in the inhibition of proteoglycan secretion in a rat glomerular culture model is the upper left panel of my August 8, 1988 laboratory notebook entry, which depicts the results of sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis of rat glomerular cell culture samples. The experiments were performed essentially as described in the Specification on pages 20 to 22, Example IV and pages 23 to 24, Example VII. Briefly, glomeruli were isolated from rat kidneys 7 days after the animal were injected with either anti-thymocyte serum to induce glomerulonephritis or with control serum. The glomeruli were seeded at  $5 \times 10^3$  glomeruli/ml in serum-free antibiotic free RPMI 1640. Lanes 2 and 3 show untreated glomerular cell culture, while lanes 4 and 5 show glomerular culture obtained from animals treated with anti-thymocyte serum. Lane 6 shows glomerular culture obtained from control animals and incubated in the presence of TGF- $\beta$ . Lane 7 shows glomerular culture obtained from control animals and incubated in the presence of TGF- $\beta$  and anti-TGF- $\beta$ . After 24 hours of incubation,

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the cultures were biosynthetically labeled by addition of 200  $\mu\text{Ci/ml}$  of  $[^{35}\text{S}]$  sulfate for an additional 24 hours as described in Example II(1) of the Specification. Subsequently, the culture medium was removed, protease inhibitors were added, and the mixture was centrifuged to remove cellular debris and electrophoresed.

6. In summary, the experimental data depicted in Exhibit D and B1, respectively, to the Rule 131 Declarations of October 1, 1996, and August 25, 1999, are accurately described in the Declarations as well as in the Exhibits themselves and were performed prior to December 22, 1988. As explained above, the upper right hand legend present in these Exhibits is not present in the corresponding original notebook entry. I added the legend, which is an accurate description of the experimental data, in order to more easily explain the data to a person unfamiliar with the experimental details and shorthand notations and abbreviations used in my laboratory notebook.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that willful, false statements may jeopardize the validity of the application or any patent issued thereon.

  
WAYNE BORDER, M.D.

10/13/01  
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DATE